REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

The claims have been amended in a manner to overcome the grounds of rejection set forth under 35 USC 112, second paragraph, of claims 2, 4, 8, 9, 10, 11 and 15. See item 9.

The Examiner's indication that claim 4 is free of the prior art is appreciated.

Claim 9 has been rejected under 35 USC 112, first paragraph, as lacking a sufficient written description and as lacking enablement for the reasons set forth in items 6 and 7 of the Action. These grounds of rejection are respectfully traversed.

The vector of claim 9 is made by inserting a heatshock promoter directed Gal4 activator domain-large T antigen fusion gene (Gal4-Large T fusion gene) into the polycloning site of the pCasperhr, and a schematic map of the vector (pCasperhs-G4-LT) is presented on Figure 3.

Therefore, artisans well understand that the starting vector (pCasperhs) has a construction of Figure 3 without the Gal4-Large T fusion gene. Further, the pCasperhs is well known in the art. Please see http://flybase.bio.indian/edu/.bin/fbidq.html?FBmc0000179, which is a website "FlyBase Report". Attached herewith is a copy of the website. The website shows the molecular map of the pCasperhs (also attached herewith) and shows references relating to the vector. In addition, please note the nucleotide full sequence of the vector was available on August 8, 1996 on GenBank database (also attached herewith).

Therefore, it is respectfully submitted that one of skill in the art can easily make the vector of claim 9 by referring to the nucleotide sequence of pCassperhs on GenBank, or to the construction on Figure 3 of this application.

Accordingly, reconsideration of both grounds of rejection is respectfully solicited.

Lastly, claims 1-3, 5-8 and 10-15 are rejected under 35 USC 103 as being unpatentable over Sands et al. in view of Thummel et al., Pirrotta et al. and Gustafson for the reasons set forth in item 11. This ground of rejection is respectfully traversed.

The Examiner pointed to the mammalian trap vector for gene-trap (Sands et al., 1996; the contents of which are basically the same as those of Zambrowicz et al., 1998, Nature, 392, 608).

The Examiner also pointed out the similarities of the Applicant's vectors with those made by Thummel, Pirrotta, and others for *Drosophila* transformation and Gal4 expression.

However, Sands et al. utilized a drug resistance gene (e.g., pupomycin) as a marker for gene-trap, and this marker was only useful in selecting clones with mutated genes in tissue culture cells. The function and expression of the respective genes were not possible to determine at the time of selection.

On the other hand, the Applicant's system allowed, for the first time, one to observe the expression and to determine the function of the mutated genes at the time of selection utilizing the whole live organism. The instant system even made it possible to isolate the lethal mutants in the gene of purpose before determination of the sequence of the mutated gene of the organism, just by recovering a survivor when the organisms subjected to screening carried the wide-type gene-X driven by the UAS sequence. This is an unprecedented feature of the claimed system that is nonobvious from the prior art.

Thummel et al. (1998) suggested the possibility to inactivate the gene at or nearby the insertion site with his Pcasper-based vectors. However, he employed gene-inactivation by generating an antisense transcript by inverting the direction of the inserted sequence in the vector. This strategy was totally unrelated to the instant method, and the antisense expression has, at least so far as the Applicant knows, not successfully inactivated the gene.

Gustafson & Boulianne used P-element vectors with Gal4 to mutate and subsequently rescue the phenotype by means of UAS-driven expression of the wild-type copy of the gene. However, as the expression of the wild-type gene in the system described by Gustafson & Boulianne was not mediated by the intrinsic promoter of the mutated gene, perfect rescue of the phenotype was not expected. In the claimed system, in contrast, the Gal4 was always transcribed by the action of the intrinsic promoter of the gene mutated, and therefore, complete rescue was attained. This is the distinct difference of the claimed system from other P-element vector systems including all described in Thummel et al., Gustafson & Bouliannc and Pirrotta et al.

In view of the foregoing, it is believed that each ground of rejection set forth in the Official Action have been overcome, and that the application is now in condition for allowance.

Accordingly, such allowance is solicited.

Respectfully submitted,

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